New Onset of Inflammatory Bowel Disease in Three Patients Undergoing IL-17A Inhibitor Secukinumab: A Case Series

New Onset of Inflammatory Bowel Disease in Three Patients Undergoing IL-17A Inhibitor Secukinumab: A Case Series

Running Head: Inflammatory Bowel Disease and Secukinumab

Marta Vernero, MD[1], Marco Astegiano, MD[1], and Davide Giuseppe Ribaldone, MD[2]

[1] Department of General and Specialist Medicine, Gastroenterologia-U, Città della Salute e della Scienza di Torino, C.so Bramante 88, 10126 Turin, Italy

[2] Division of Gastroenterology, Department of Medical Sciences, Molinette Hospital, University of Turin, Italy

Corresponding author: Davide Giuseppe Ribaldone, Department of Medical Sciences, Division of Gastroenterology, Università di Torino, C.so Bramante 88 - 10126 Turin – Italy. E-mail: davrib_1998@yahoo.com Tel: +390116333918, Fax: +390116333623.

word count: 474

Keywords: Crohn's Disease; Ulcerative Colitis; IL-17a Inhibitor; Secukinumab; Permeability

CONFLICT OF INTEREST/STUDY SUPPORT:

1. The author acting as the submission's guarantor is Davide Giuseppe Ribaldone

2. Davide Giuseppe Ribaldone conceived and revised the paper; Marta Vernero written the paper; Marco Astegiano revised the paper; the authors approved the final draft submitted.

3. No financial support to declare.

4. Conflict of interest: none to declare.

PATIENT CONSENT

All patients reported in this paper provided an informed consent form allowing the publication of their data.

Commentato [D1]: Vedi questa frase dove va messa e come va formulata secondo le regole della rivista

To the Editor: We recently detected an alarming series of cases of suspected new diagnoses of inflammatory bowel disease (IBD) in patients receiving secukinumab.

Secukinumab is an IL-17A neutralizing antibody widely used in dermatological and rheumatological diseases (1).

Commentato [MV2]: Non sono sicura di poter usare questa citazione, ma l'ho trovata in un altro articolo quindi penso di si.

Commentato [D3R2]: Elimina questo commento

In the last 6 months 5 patients were referred to our IBD ambulatory for evaluation of abdominal pain and diarrhea after receiving secukinumab and three of them were diagnosed with IBD. Main features of the patients are reported in table 1.

Table 1.

Commentato [D4]: Vedi dove vanno messe le tabelle

The first patient was referred from another hospital for onset of bloody diarrhea after a 12-month therapy with secukinumab for plaque psoriasis unresponsive to adalimumab and etanercept. A colonoscopy was performed showing an active inflammation of the rectum and sigmoid colon confirmed by crypt distortion and abscess seen through histological examination. Secukinumab was suspended and the patient was successfully treated with intravenous steroids. After three months their disease relapsed: a second colonoscopy was performed confirming the diagnosis of active extensive ulcerative colitis (UC). As psoriasis was worsening, the patient was evaluated both from gastroenterologist and dermatologist and we are planning to start ustekinumab soon.

A second patient reported onset of non-bloody diarrhea and abdominal pain after 5-months of therapy with secukinumab for ankylosing spondylitis. A colonoscopy with histological examination showed a segmental chronical inflammation of the bowel, suggestive of IBD.

We decided to stop secukinumab administration and to prescribe systemic oral steroids. Three months later the patient was in clinical remission.

Regarding patient 3, he was referred to us because of onset of IBD while undergoing secukinumab for psoriasis unresponsive to immunosuppressant and anti TNF drugs; he was first admitted to another hospital for non-bloody diarrhea, abdominal pain, vomiting and weight loss; the patient reported starting secukinumab three months before symptoms onset. Colonoscopy showed extensive colonic inflammation and histological examination was suggestive of IBD. After stopping secukinumab the patient was treated with adalimumab with no benefit. Due to the severe activity of both IBD and psoriasis we decided to start ustekinumab with good results on dermatological and gastroenterological symptoms.

Although IL-17 is believed to be one of the pro-inflammatory cytokines involved in pathogenesis of IBD (2), a few cases of worsening or new onset of IBD in patients undergoing IL17A inhibitor have been reported (3, 4). Moreover, during secukinumab clinical trials on psoriasis 3 ulcerative colitis (UC) and 1 Crohn's disease (CD) were reported among treatment group (whereas in the placebo group no cases of IBD were detected) (5).

The IBD incidence seen in these studies may in part be related to the underlying correlation between IBD and psoriasis, psoriatic arthritis and ankylosing spondylitis, but the possibility that IBD is an adverse effect of the biologic itself cannot be excluded. This arouses important thoughts about the etiopathogenesis of IBD: the complete block of the action of IL-17A could contribute to the leaky intestinal epithelium found in IBD (3)?

Commentato [D5]: Nuovi casi o recidiva in già noti?

Commentato [MV6R5]: Casi nuovi

Commentato [MV7]: RICORDA: sposta tabella e fai titolo

Commentato [D8R7]: Cancella commento

REFERENCES

1. Nash P, McInnes IB, Mease PJ, *et al*. Secukinumab Versus Adalimumab for Psoriatic Arthritis: Comparative Effectiveness up to 48 Weeks Using a Matching-Adjusted Indirect Comparison. Rheumatol. Ther. 2018;5:99-122.

2. Strober W, Fuss IJ. Proinflammatory cytokines in the pathogenesis of inflammatory bowel diseases. Gastroenterology 2011;140:1756-1767.
3. Wang J, Bathia A, Cleveland NK, *et al*. Rapid Onset of inflammatory bowel disease after receiving Secukinumab infusion. ACG Case Rep. J. 2018;5:e56.
4. Ehlich D, Jamaluddin N, Pisegna J, *et al*. A challenging case of severe ulcerative colitis following the initiation of secukinumab for ankylosing spondylitis. Case Rep. Gastrointest. Med. 2018;2018:9679287.
5. Langley RG, Elewski BE, Lebwohl M, *et al*. Secukinumab in plaque psoriasis-results of two phase 3 trials. N. Eng. J. Med. 2014;371:326-338.

Commentato [MV9]: Non so se si debba mettere anche: doi: 10.14309/crj.2018.56.eCollection2018
Non c'erano esempi di riviste online nelle indicazioni sulla bibliografia

Commentato [D10R9]: No

Commentato [MV11]: Anche qui era un po' strana la citazione. C'è anche qui il doi: 10.1155/2018/9679287.eCollection2018.

Commentato [D12R11]: E' ok

Table 1. Characteristics of the patients

AGE	SEX	DISEASE	FAMILY HISTORY OF IBD?	SMOKER?	GI SYMPTOMS BEFORE SECUKINUMAB?	HISTOLOGICALLY CONFIRMED IBD?
27	F	Plaque psoriasis	no	no	no	Yes
46	F	Ankylosing spondylitis	no	no	no	Yes
33	M	Psoriatic arthritis	no	no	no	Yes

F = female; M = male